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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,034	10/11/2001	Kin-Ming Lo	LEX-009DV	4315

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TESTA, HURWITZ & THIBEAULT, LLP
HIGH STREET TOWER
125 HIGH STREET
BOSTON, MA 02110

EXAMINER	
JIANG, DONG	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/05/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/977,034	LO ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- Th MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's preliminary amendment in paper No. 5, filed on 11 October 2001 is acknowledged and entered. Following the amendment, claims 1-25 are canceled, claims 26 and 27 are amended, and the new claims 30-38 are added.

Currently, claims 26-38 are pending and under consideration.

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 is indefinite because no amount is indicated. Insertion of "an effective amount of" after "mammal" at line 2 of the claim would be remedial.

Claim 27 is similarly indefinite.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26, 28-30, 34-36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al., US 5,723,125, taken with Lo et al., US5,541,087 (both are provided by applicants).

Chang discloses that IFN-α has been approved for indications such as hepatitis B and C (column 1, lines 22-26). Additionally, Chang teaches that IFN-α has short circulation half life, that to use IFN-α as an effective systemic therapeutic, one needs large doses and frequent administration, which are inconvenient, painful, and toxic (column 1, lines 28-46). Further, Chang teaches that to overcome these disadvantages, one can modify the molecule to increase its circulation half life (column 1, lines 46-48), and that IgG has been found to increase the half lives of several ligand binding proteins when used to form recombinant hybrids (column 1, line 65 to column 2, line 3).

Lo discloses a fusion protein expression system comprising, from its 5' to 3' direction, a signal sequence, an immunoglobulin Fc region, and target protein sequence, and indicates that the system is generally useful for protein expression in mammalian cells as it enhances the production of a given target protein (column 1, the first paragraph), and can be adapted to facilitate recombinant production of *any* desired target protein (column 8, lines 1-6). Additionally, Lo teaches that if the fusion protein is to be used as a biopharmaceutical, the Fc domain may confer the effector function activities to the fusion protein, such as a longer serum half-life (column 3, lines 1-7). Further, Lo teaches that the Fcγ1 region includes at least a portion of the hinge domain, and CH3 domain, or at least a portion of the hinge domain, CH2 and CH3 domains (column 2, lines 60-63).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a fusion Fc-IFN-α protein following the teachings of Lo for treating a condition such as hepatitis because, as taught by Chang, IFN-α is known for the treatment of hepatitis, and the hybrid Fc-IFN-α would have the advantage of prolonged serum half life according to the teachings of Lo and Chang. The person of ordinary skill in the art would have been motivated to use the hybrid Fc-IFN-α for the treatment of diseases such hepatitis, and reasonably would have expected success because many proteins in the form of Fc fusion have been proven in the art to have prolonged in vivo half life as indicated by both Chang and Lo.

With respect to the limitation of "a fusion protein that binds a Fc receptor expressed on a target cell", when the hybrid Fc-IFN-α is used to treat a condition such as hepatitis, it would inherently bind to a Fc receptor.

Claims 27, 31-33 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al., US 5,723,125, and Lo et al., US5,541,087, as applied to claims 26, 28-30, 34-36 and 38 above, and further in view of Capon et al., US5,116,964 (provided by applicants).

The teachings of Chang and Lo are reviewed above. Neither reference specifically teaches a multimeric protein comprising at least two fusion proteins.

Capon discloses a novel polypeptide comprising an immunoglobulin Fc region and a target protein sequence (column 5, lines 13-20), and a polypeptide comprising multimeric fusion proteins with various combinations (column 5, lines 40-43, column 10, the fourth paragraph, and column 12, lines 1-4, and 60-64), which molecules become capable of binding and/or activating more than one ligand (column 4, lines 52-56). Additionally, Capon teaches that fusion of a target protein to a stable plasma protein such as an immunoglobulin constant domain extends the in vivo plasma half-life, and facilitate purification of the protein (column 4, lines 38-43, and column 5, lines 13-20).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a multimeric protein comprising at least two fusion Fc-IFN-α molecules following the teachings of Lo and Capon for treating a condition such as hepatitis

because, as taught by Chang, IFN-α is known for the treatment of hepatitis, the hybrid Fc-IFN-α would have the advantage of prolonged serum half life according to the teachings of Lo, Chang and Capon, and a multimer would have higher efficacy as it would be capable of binding and activating more than one receptor. The person of ordinary skill in the art would have been motivated to use the multimeric hybrid Fc-IFN-α in the treatment of diseases such hepatitis, and reasonably would have expected success in view of Capon's disclosure.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
4/28/03